AF

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,472	01/14/2000	HIROSHI MATSUI	0010-1075-0-	5130

22850 7590 10/20/2005

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 10/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/462,472	MATSUI ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22,25 and 27* is/are pending in the application.

4a) Of the above claim(s) *1-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-22,25 and 27* is/are rejected.

7)☒ Claim(s) *13-22 and 25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *1/14/2000* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 13-22, 25, and 27 under consideration in this Office Action.

2. The rejection of claims 14-22 and 25 under 35 U.S.C. 112, second paragraph, as being indefinite has been withdrawn in view of applicants' amendment to the claims filed on03/22/2004.

Claim Objections

3. Claims 13-22 and 25 are objected to because of they recite non-elected subject matter.

Applicants' arguments filed 03/22/2004 have been fully considered but they are not persuasive in view of petition decision dated 11/16/2004. Of particular relevance is page 5 of the petition dated 11/16/2004 which is reproduced below:

> "Applicants' arguments are not persuasive as the examination standard provided by MPEP 803.02 does not apply to PCT. According to Administration Instructions, Annex-, Part B, the species election between the enzymes can be maintained even though they all belong to a recognized class of chemical compounds because all the enzymes claimed do not fulfill the following criteria:
>
> - all of the enzymes do not share a common structure and at least one Markush alternative is not novel over the prior art. Specifically, Seeger et al. (copy enclosed) teach the enzyme xanthosine phosphorylase as claimed and Mori et al. (copy enclosed) teach the enzyme inosine-guanosine kinase as claimed."

In view of the petition decision dated 11/16/2004, applicants are required to cancel or amend the claims to recite the elected subject matter of phosphoglucose isomerase.

Furthermore, claim 13 is objected to since it recites "phophoglucose isomerase" which is incorrectly spelled. Correction of this misspelling is required.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 13-22, 25, and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the evaluation of the claims for compliance with the written description requirement of 35 U.S.C. 112, of particular relevance is 66 FR 1099, Friday, January 5, 2001,which states:

> "*Eli Lilly* explains that a chemical compound's name does not necessarily convey a written description of the named chemical compound, particularly when a genus of compounds is claimed. *Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1405. The name, if it does no more than distinguish the claimed genus from all others by function, does not satisfy the written description requirement because "it does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. *Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1406. Thus *Eli Lilly* identified a set of circumstances in which the words of the claim did not, without more, adequately convey to others that applicants had possession of what they claimed." (see p. 1100, 1st column, line 47 to 2nd column, line 2).

The claims are drawn to a method comprising the use of a genus of phosphoglucose isomerase, a genus of phosphoribosyl pyrophosphate amidotransferases, a genus of phosphoribosyl pyrophosphate synthetases, a genus of purine repressors encoded by the purR gene, a genus of nucleoside permeases, and their respective mutants and variants. The scope of each genus includes many members with widely differing structural, chemical, and physiochemical properties including widely differing amino acid sequences. Furthermore, each genus is highly

variable because a significant number of structural differences between genus members exists.

The recitation of the name "phosphoglucose isomerase", "phosphoribosyl pyrophosphate amidotransferase", or "phosphoribosyl pyrophosphate synthetase" does not define any structural features and amino acid sequences commonly possessed by each genus. Furthermore, the specification does not describe and define any structural features and amino acid sequences commonly possessed by the genus. Thus, one skilled in the art cannot visualize or recognize the identity of the members of each genus for use in the claimed method.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v, Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Therefore, the instant claims are not adequately described.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of a genus of phosphoglucose isomerase, a genus of phosphoribosyl pyrophosphate amidotransferases, a genus of phosphoribosyl pyrophosphate synthetases, a genus of purine repressors encoded by the purR gene, and a genus of nucleoside permeases.

6. Claims 16 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass any phosphoribosyl pyrophosphate amidotransferase or phosphoribosyl pyrophosphate synthetase that has desensitization of feedback inhibition due to any genetic mutation in any encoding polynucleotide. However, the specification does not provide guidance, prediction, and working examples for making any phosphoribosyl pyrophosphate amidotransferase or phosphoribosyl pyrophosphate synthetase that has desensitization of feedback inhibition, where any genetic mutation in any encoding polynucleotide is encompassed by the claims.

Thus, an undue amount of trial and error experimentation must be preformed to search and screen for any type of genetic mutation to the encoding polynucleotide including nucleotide deletion, insertion, addition, substitution, or combinations thereof. General teaching regarding screening and searching for the claimed invention using enzyme activity assays is not guidance for making the claimed invention.

In view of the above considerations, the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim Rejections - 35 U.S.C. § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims [13, 27] are rejected under 35 U.S.C. 103(a) as being unpatentable over Mascarenhas et al. (Appl Environ Microbiol. 1991 Oct;57(10):2995-9) in view of Gelpi. (.J Chromatogr A. 1995 May 26;703(1-2):59-80).

Mascarenhas et al. teach a fermentation process comprising culturing in a culture media *E.coli* cells comprising a deletion of the *pgi* gene encoding phosphoglucose isomerase (see entire publication).

Gelpi teach liquid chromatography-mass spectrometry analysis applications for identifying

and quantifying nucleosides (see entire publication).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the process taught by Mascarenhas et al. by collecting the produced purine nucleoside and then subjecting it to liquid chromatography-mass spectrometry analysis as taught by Gelpi in order to identify and measure the amount of the produced purine nucleoside.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this for the purposes of making a beneficial process that produces purine nucleosides and as an alternative to a chemical synthesis of purine nucleosides.

No patentable weight is given to the preamble of these process claims since it merely recites the purpose of these process claims. Because the process steps of the modified Mascarenhas et al. are the same as the process steps of the claimed invention then the modified Mascarenhas et al. process would inherently produce and accumulate purine nucleosides.

9. Claims 14, 15, 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mascarenhas et al. in view of Gelpi as applied to claims 13 and 27 above, and further in view of Neuhard et al (reference of record).

Neuhard et al . teach the *E.coli prs* gene encoding phosphoribosyl pyrophosphate synthetase which is involved in the biosythesis of purine nucleoside (see entire publication, especially pp. 447-448).

Neuhard et al. further teach the *E.coli purF* gene encoding phosphoribosyl pyrophosphate amidotransferase which is involved in biosynthesis of purine nucleoside (see entire publication, especially pp. 448-452; Fig 1; and Table 4).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further modified the modified Mascarenhas et al. process stated above such by linking the *E.coli prs* or *purF* gene to a constitutively active promoter and transforming the *E.coli* cells with this construct to thereby overexpress phosphoribosyl pyrophosphate synthetase or phosphoribosyl pyrophosphate amidotransferase in the *E.coli* cells. One of ordinary skill in the art at the time the invention was made would have been motivated to do this since Neuhard et al . teach that these enzymes are involved in the biosythesis of purine nucleoside and that overexpression of these enzyme would sequester more substrates (e.g., ATP and ribose 5-phosphate) toward production of purine nucleosides instead other metabolites.

10. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mascarenhas et al. in view of Gelpi and Neuhard et al., as applied to claims 14, 15, 17-21 above, and further in view of Rolfes et al. (J Biol Chem. 1988 Dec 25;263(36):19653-61).

Rolfes et al. teach the *E.coli purR* gene encoding a repressor for the *E.coli purF* gene encoding phosphoribosyl pyrophosphate amidotransferase (see entire publication).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further modified the modified Mascarenhas et al. process stated above such that the *E.coli purR* gene encoding a repressor for the *E.coli purF* gene is inactivated and/or deleted. One of ordinary skill in the art at the time the invention was made would have been motivated to do this for the purposes of allowing overexpression of phosphoribosyl pyrophosphate amidotransferase thereby sequestering more substrates toward production of purine nucleosides instead other metabolites.

11. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mascarenhas et al. in view of Gelpi as applied to claims 13 and 27 above, and further in view of Accession P09452 (01-MARCH-1989).

Accession P09452 teaches the *E.coli nupG* gene encoding the nucleoside permease nupG (see attached report).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further modified the modified Mascarenhas et al. process stated above such that the *E.coli nupG* gene encoding the nucleoside permease nupG is inactivated and/or deleted. One of ordinary skill in the art at the time the invention was made would have been motivated to do this for the purposes of preventing the *E.coli* cells from transporting the produced purine nucleoside into the cell where it could be metabolized.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

14. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600